Am J Obstet Gyn 152: 116-117

May 1, 1985
Am J Obstet Gynecol

ence of a circle [(D1 + D2) 1.57] was clinically useful when deriving gestational age from the head circumference except when an abnormal cephalic index of <79% with a biparietal diameter >7 cm.

2. We take no credit for the "correctness" of the equation for the circumference of an ellipse. This was the reason for referring to *Scientific Tables*. We can only assume that the editors of this particular reference thought that there was no difference between the equation for the circumference of an ellipse which they used and the "true equation" referred to by the authors of the above letter.

3. Our only criticism of the above letter is that the authors did not represent their data in a similar format as illustrated in Fig. 2 of our article, for it can be seen that for a given cephalic index, the error in estimating gestational age from the head circumferences increases as the biparietal diameter increases. If they had done this, perhaps they might have been more revealing as to the clinical significance of their communication.

Greggory R. DeVore, M.D.
Womens Hospital
Los Angeles County/University
of Southern California Medical Center
5K40
1240 North Mission Road
Los Angeles, California 90033

Mumps and postmenopausal ovarian cancer

To the Editors:

In the article entitled "Mumps, menarche, menopause, and ovarian cancer" (Cramer DW, Welch WR, Cassells S, Scully RE. AM J OBSTET GYNECOL 1983; 147:1-6) Cramer et al. suggest that mumps infection may increase the risk of postmenopausal ovarian cancer via a causal chain thought to include inapparent oophoritis, oocyte depletion, and resultant premature menopause. They present evidence from a case-control interview study to support their hypothesis, which they outline more fully in another publication.[1]

We have attempted to reproduce the findings of Cramer et al. in data collected as part of a similar case-control interview study of ovarian cancer. Our case series included 298 women with pathologically confirmed primary ovarian cancer of the epithelial type who were treated at 33 participating hospitals in the Washington, D. C., area. The controls were 344 women treated at the same hospitals for conditions presumed to be unrelated to the exposures under study. Excluded conditions included gynecologic disease, gallbladder complaints, ischemic cardiovascular disease, colon cancer, melanoma, and pregnancy. The controls were frequency-matched to cases on age, race, and hospital. To promote comparability with the study of Cramer et al., we have restricted the present analysis to 147 white case women reporting a natural menopause and to 152 corresponding control women.

In Table I, mumps history data from the two studies are presented for comparison. Cramer et al. found a significant excess of uncertain mumps histories among their case women compared to controls. They postulated that this excess might represent increased inapparent mumps oophoritis among cases. In contrast, our subjects were much more certain of their mumps history than were the subjects of Cramer et al. Among the few women who could not recall whether they had had mumps, cases and controls were equally represented. These two observations argue against the importance of an "uncertain" mumps history.

We did find, in agreement with Cramer et al., that among subjects reporting a positive mumps history, more cases (20%) than controls (13%) were initially unsure of their age at exposure. However, in our study a follow-up question allowed these subjects to date their mumps history more broadly, using four age categories. The group unable to date their exposure was reduced to only five (three cases, 2 controls). The explanation for this finding is unclear; overall, we believe that an uncertain mumps history is more likely to be a result of interviewing method than a suggestion of inapparent mumps infection.

As part of their hypothesis, Cramer et al. suggest that silent mumps infection causes premature ovarian failure. Our data do not support this conclusion. Control women with a negative or uncertain mumps history reported a later average menopause (49.3 ± 0.5) than control women with a positive mumps history (48.7 ± 0.5).

Cramer et al. found a significant negative correlation

Table I. Clinical history of mumps for postmenopausal case subjects with ovarian cancer and for corresponding control subjects in two studies

	Washington, D.C., case-control study				*Cramer et al. (1983)*			
	Cases		*Controls*		*Cases*		*Controls*	
Clinical history of mumps	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Negative								
Never had	41	27.9	38	25.0	26	21.9	24	22.0
Unknown whether had	9	6.1	10	6.6	33	27.7	17	15.6
Positive								
Had, age known	67	45.6	85	55.9	10	8.4	30	27.5
Had, age unknown	30	20.4	19	12.5	50	42.0	38	34.9
Total	147	100.0	152	100.0	119	100.0	109	100.0

between age at menarche and age at menopause among both case and control women who recalled having had mumps. In contrast, we observed a nonsignificant positive correlation in both groups. The strongest negative correlation seen by Cramer et al. was among nulliparous white case women who recalled having mumps; among the 24 subjects in this subgroup we found a significant ($p = 0.001$) positive Pearson's correlation coefficient of 0.62. Our correlational results, combined with those of Cramer et al., suggest that the significant correlations found in either study may represent artifactual findings caused by extensive subgroup analysis.

In summary, our results do not support the hypothesis of Cramer et al. However, we agree with the authors that mumps history is an inadequate measure of exposure. To further clarify the relation of mumps infection to ovarian cancer, serologic techniques such as enzyme-linked immunosorbent assay must be used. Of course, even when accurate serologic techniques are used, oophoritis caused by inapparent mumps infection remains an unmeasurable entity, so this aspect of the hypothesis by Cramer et al. cannot be tested at present.

Mark H. Schiffman, M.D., M.P.H.
Patricia Hartge, Sc.D.

Environmental Studies Section
Environmental Epidemiology Branch
National Cancer Institute
Landow Building, Room 3C06
7910 Woodmont Avenue
Bethesda, Maryland 20205

Linda P. Lesher, M.H.S.
Larry McGowan, M.D.

Division of Gynecologic Oncology
Department of Obstetrics and Gynecology
George Washington University Medical Center
2150 Pennsylvania Avenue, N.W.
Washington, D. C. 20037

REFERENCE

1. Cramer DW, Welch WR. Determinants of ovarian cancer risk. II. Inferences regarding pathogenesis. JNCI 1983; 71:717-720.

Reply

To the Editors:

Table I compares the results of published case-control studies[1-4] on the relationship of clinical history of mumps parotitis and ovarian cancer with the data offered by Schiffman et al. Two points are worthy of comment. First, all of the studies demonstrate an excess of controls over cases who have a positive clinical history of mumps parotitis and conversely an excess of cases over controls with a negative clinical history. An earlier study by West[5] also reported this finding (with a statistical significance of 0.007), but details on the numbers and proportions were not provided. The second point is that the data of Schiffman et al. stands out as having the smallest difference between cases and controls, 2% compared to the 10% to 18% found in the other studies. The atypicality of their data in this respect should be considered in weighing the evidence against the mumps hypothesis offered by their data.

Perhaps Schiffman et al. are correct in their assertion that the association of mumps history with ovarian cancer is a result of interviewer bias, but the fact that repeated independent studies have found differences suggests to us that the association is real. We certainly concede that clinical history of mumps is an inadequate measure of a woman's actual experience with mumps. Like Schiffman et al., we despair that case-control studies, even with use of sensitive antibody studies, will ever be able to distinguish past oophoritis from parotitis. Perhaps the best we can hope for is that a suitable animal model may be found to demonstrate the long-term effect of mumps on ovaries.

In conclusion, the data presented by Schiffman et al. do not compel us to change the major elements of our hypothesis, which were as follows: (1) Women with ovarian cancer differ in some way in their past experience with mumps infection from other women. (2) A possible interpretation of this difference is that women with ovarian cancer have more frequently suffered unapparent mumps oophoritis. (3) Since mumps oophoritis has been linked to premature ovarian failure, the mumps virus could be linked to ovarian cancer in the

Table I. Comparison of case-control studies* on the relationship of clinical history of mumps parotitis and ovarian cancer with the data of Schiffman et al.

	Positive clinical history				*Negative clinical history*			
	Cases		*Controls*		*Cases*		*Controls*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Newhouse et al.[1]	128	43	318	53	172	57	282	47
Menczer et al.[2]	25	36	29	49	44	64	30	51
Golan et al.[3]	13	38	19	56	21	62	15	44
Cramer et al.[4] (postmenopausal subjects)	60	50	68	62	59	50	41	38
Shiffman et al. (postmenopausal subjects)	97	66	104	68	50	34	48	32

*Numbers of subjects inferred from proportions stated in text.

same way that agents that induced ovarian failure in animals also produced ovarian tumors.

Daniel W. Cramer, M.D., Sc.D.
Department of Obstetrics and Gynecology
Brigham and Women's Hospital
75 Francis Street
Boston, Massachusetts 02115

REFERENCES

1. Newhouse ML, Pearson RM, Fullerton JM, Boesen EA, Shannon HS. A case control study of carcinoma of the ovary. Br J Prev Soc Med 1977;31:148-53.
2. Menczer J, Modan M, Ranon L, Golan A. Possible role of mumps virus in the etiology of ovarian cancer. Cancer 1979;43:1375-9.
3. Golan A, Joosting AC, Orchard ME. Mumps virus and ovarian cancer. S Afr Med J 1979;56:18-21.
4. Cramer DW, Welch WR, Cassells S, Scully RE. Mumps, menarche, menopause, and ovarian cancer. AM J OBSTET GYNECOL 1983;147:1-6.
5. West RO. Epidemiologic study of malignancies of the ovaries. Cancer 1966;19:1001-7.

Erratum

In the April 1, 1984, issue of the JOURNAL, in the article by Fabro, McLachlan, and Dames, entitled "Chemical exposure of embryos during the preimplantation stages of pregnancy: Mortality rate and intrauterine development," on page 929, the following footnotes should have appeared:

A large portion of this work was carried out in the Department of Pharmacology, The George Washington University Medical Center, Washington, D. C., and was supported by United States Public Health Service Research Grant GM13749 from the National Institute of General Medical Sciences, National Institutes of Health. J. A. M. and N. M. D. were trainees supported by Training Grant GM26.

Portions of this work are from a dissertation by J. A. M. and a thesis by N. M. D. presented to the Department of Pharmacology, The George Washington University Graduate School of Arts and Sciences, in partial fulfillment of the requirements for the Ph.D and M.S. degrees, respectively.